

**Amendments to the Drawings:**

The attached replacement drawing sheets makes changes to Figs. 1, 2D, 3, 4A, 4B, 5A, 5B, and 6 and replace the original sheets with Figs. 1, 2D, 3, 4A, 4B, 5A, 5B, and 6.

Attachment: Replacement Sheets

**REMARKS**

Claims 1-11 and 13-23 are pending in this application. Non-elected claims 18-21 have been withdrawn from consideration by the Examiner. By this Amendment, the specification, claims 1-4, 7-9, 13-17, 20, and 22, and Figs. 1, 2D, 3, 4A, 4B, 5A, 5B, and 6 are amended; claim 12 is canceled; and claim 23 is added. Support for the amendments may be found, for example, in the originally filed specification and claims. In addition, the specification is amended herein to replace the Sequence Listing filed February 27, 2007 with the attached substitute Sequence Listing. Support for the substitute Sequence Listing is found, for example, in the originally filed specification. No new matter is added.

In view of the foregoing amendments and following remarks, Applicants respectfully request reconsideration and allowance.

**I. Personal and Telephone Interviews**

The courtesies extended to Applicants' representative by Examiner Parkin at the personal interview held December 1, 2009, and during the telephonic interview held December 15, 2009, are appreciated. The reasons presented at the interviews as warranting favorable action are incorporated into the remarks below, which constitute Applicants' record of the interviews.

**II. Information Disclosure Statement**

The Office Action does not consider references 8 and 10 listed on the PTO-1449 of the Information Disclosure Statement (IDS) filed on October 20, 2009. Although these references are not in English, they were cited in a foreign search report. An English-language version of a foreign search report was filed in the IDS as a statement of relevance for references 8 and 10. Applicants respectfully request consideration of these references.

### **III. Amendments to the Specification and Sequence Listing**

By this Amendment, and as discussed during the interviews, various paragraphs in the specification are amended to add appropriate headings, add a Brief Description of the Drawings, eliminate informalities, to correct amino acid numberings due to an incorrectly listed reading frame in the figures with respect to the isolate HIV-1 HxB2, and to correct the misuse of the term "between" when describing oligonucleotide sequences that are replaced.

Also, after review, the strains used in this application were added and clarified as discussed during the interviews. Specifically, the 32 strain-consensus sequence of Fig. 2A corresponds with the sequence of isolate ENV\_HV1BR (Swiss-Prot P03377) and the sequence used in Fig. 3 (SEQ ID NO:14) was derived from isolate ENV\_HV1LW (Swiss-Prot Q70626). These isolates correspond exactly with the sequences listed in the original disclosure. Copies of the Swiss Protein Database documents for each of the above isolates are attached.

In addition, Applicants submit herewith a publication (Back et al.) establishing that the HxB2 sequence was known in the art at the time of invention.

The attached paper copy and computer-readable copy of the Sequence Listing are submitted in compliance with 37 C.F.R. §§1.821-1.825. The contents of the paper copy and the computer-readable copy of the Sequence Listing are the same.

No new matter is added. Applicants respectfully request entry and consideration of the amendments.

### **IV. Amendments to the Drawings**

By this Amendment, Figs. 1, 2D, 3, 4A, 4B, 5A, 5B, and 6 are amended to correct various errors. Figs. 1, 3, 4A, 4B, 5A, 5B, and 6 are amended to correct the numbering to correspond with HIV-1 HxB2 which begins with amino acid 540, as opposed to amino acid

472. The specification at page 5 references HxB2 as the isolate, however, for unknown reasons, the reading frame was incorrectly labeled.

Fig. 2D is amended to (1) delete amino acid 603 ("C"), which was erroneously included in the oligonucleotide sequence, (2) replace "13" with "12," (3) replace "Region 603-615" with "Region 604-615," and (4) to correct the typographical error of "558" by replacing it with "598." Support for these amendments may be found, for example, in the originally filed Fig. 1 and the specification at page 8, lines 1-8.

In addition, Fig. 3 is amended to correct amino acid 539, which was erroneously listed as M, but is known to be V.

No new matter is added. Applicants respectfully request entry and consideration of the amended drawings.

**V. 35 U.S.C. §112, Second Paragraph Rejection**

The Office Action rejects claims 1-17 and 22 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. By this Amendment, claim 12 is canceled, rendering its rejection moot. As discussed during the interviews, the remaining claims are variously amended, as set forth *supra*, to obviate the issues presented in the Office Action. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

**VI. 35 U.S.C. §112, First Paragraph Rejections**

**A. Claims 1-17**

The Office Action rejects claims 1-17 under the enablement requirement of 35 U.S.C. §112, first paragraph. By this Amendment, claim 12 is canceled, rendering its rejection moot. As to the remaining claims, Applicants respectfully traverse the rejection.

Any analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether the disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention without undue experimentation. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). In order to make an enablement rejection, the Examiner has the initial burden to establish a reasonable basis to question the enablement provided by the claimed invention. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). As stated by the court:

It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosures.

As discussed during the interviews, IDRs for gp41 are well known and identified in the art. A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). The specification at page 5, lines 4-8, defines IDR for purposes of this application. In addition, Applicants submit herewith two publications (Earl et al. 1997 and Xu et al. 1991) that clearly map the epitopes of the gp41 proteins. The instant disclosure coupled with what was known in the art at the time of invention, enables one of skill in the art to make/use/practice the claimed invention without undue experimentation.

As discussed during the interviews, the disclosure and what was known in the art also provides suitable guidance to enable one of skill in the art to make/use/practice claims 9 and 10, specifically to engineer mutations that prevent cross-reactivity of B-cells and T-cells with host proteins (e.g. IL-2) and the modified polypeptide. In particular, US 6,455,265 to Serres

("Serres"), incorporated by reference, discloses mutations that impact the desired change in antigenicity and methods of identifying such mutations. See, e.g., Serres at Abstract and claim 1.

**B. Claim 22**

The Office Action rejects claim 22 under the enablement requirement of 35 U.S.C. §112, first paragraph. By this Amendment, claim 22 is amended according to the Examiner's helpful comments to recite an "immunogenic composition."

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For at least the above reasons, claims 1-11 and 13-17 and 22 are enabled by the disclosure coupled with what was known in the art at the time of invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections.

**VII. New Claim**

By this Amendment, new claim 23 is presented. New claims 23 depends from claim 1. Applicants respectfully request prompt examination and allowance of new claim 23.

**VIII. Rejoinder**

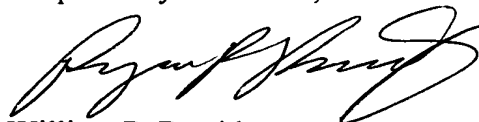
Applicants also respectfully request rejoinder of non-elected claims 18-21. Each of these claims variously depends from claim 1 and, as such, unity of invention exists between all of the claims. Because claim 1 is believed to be allowable for at least the reasons presented above, Applicants respectfully request withdrawal of the Restriction Requirement and rejoinder of claims 18-21.

**IX. Conclusion**

In view of the foregoing, Applicants respectfully submit that this application is in condition for allowance. Applicants earnestly solicit favorable reconsideration and prompt allowance of the application.

Should the Examiner believe that anything further would be desirable to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,



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WPB:RRB/rrb

Attachments:

-Earl et al., Epitope Map of Human Immunodeficiency Virus Type 1 gp41 Derived from 47 Monoclonal Antibodies Produced by Immunization with Oligomeric Envelope Protein, Journal of Virology, Vol. 71, No. 4, pp. 2674-2684, April 1997.

-Xu et al., Epitope Mapping of Two Immunodominant Domains of gp41, the Transmembrane Protein of Human Immunodeficiency Virus Type 1, Using Ten Human Monoclonal Antibodies, Journal of Virology, Vol. 65, No. 9, pp. 4832-4838, September 1991.

-Back et al., Mutations in Human Immunodeficiency Virus Type I gp41 Affect Sensitivity to Neutralization by gp120 Antibodies, Journal of Virology, Vol. 67, No. 11, pp. 6897-6902, November 1993.

-UniprotKB/Swiss-Prot P03377 (ENV\_HV1BR)

-UniprotKB/Swiss-Prot Q70626 (ENV\_HV1LW)

-Replacement Sheets

-Sequence Listing (computer-readable and paper copies)

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